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Perspective

Physician-scientists, with in-depth training in both medicine and research, are uniquely poised to address pressing challenges at the forefront of biomedicine. In recent years, a number of organizations have outlined obstacles to maintaining the pipeline of physician-scientists, classifying them as an endangered species. As in-training and early-career physician-scientists across the spectrum of the pipeline, we share here our perspective on the current challenges and available opportunities that might aid our generation in becoming independent physician-scientists. These challenges revolve around the difficulties in recruitment and retention of trainees, the length of training and lack of support at key training transition points, and the rapidly and independently changing worlds of medical and scientific training. In an era of health care reform and an environment of increasingly sparse NIH funding, these challenges are likely to become more pronounced and complex. As stakeholders, we need to coalesce behind core strategic points and regularly assess the impact and progress of our efforts with appropriate metrics. Here, we expand on the challenges that we foresee and offer potential opportunities to ensure a more sustainable physician-scientist workforce.

Challenges and opportunities for reinvigorating the physician-scientist pipeline

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Physician-scientists, with in-depth training in both medicine and research, are uniquely poised to address pressing challenges at the forefront of biomedicine. In recent years, a number of organizations have outlined obstacles to maintaining the pipeline of physician-scientists, classifying them as an endangered species. As in-training and early-career physician-scientists across the spectrum of the pipeline, we share here our perspective on the current challenges and available opportunities that might aid our generation in becoming independent physician-scientists. These challenges revolve around the difficulties in recruitment and retention of trainees, the length of training and lack of support at key training transition points, and the rapidly and independently changing worlds of medical and scientific training. In an era of health care reform and an environment of increasingly sparse NIH funding, these challenges are likely to become more pronounced and complex. As stakeholders, we need to coalesce behind core strategic points and regularly assess the impact and progress of our efforts with appropriate metrics. Here, we expand on the challenges that we foresee and offer potential opportunities to ensure a more sustainable physician-scientist workforce.

Introduction

The concept of the physician-scientist was elaborated over a century ago by Samuel Meltzer during his presidential address at the first meeting of the Association for the Advancement of Clinical Research (now the American Society for Clinical Investigation) (1). He said researchers in the science of clinical medicine "must have a training fitting them to carry out investigations in conformity with the requirements existing in all pure sciences" and that "clinical science will not thrive through chance investigations by friendly neighbors from the adjoining practical and scientific domains" (1). Eighty-three years later, Edward Benz struck an optimistic tone about the future of the physician-scientist enterprise, stating, "All too often, we incorrectly lead people to believe that we are teetering on the brink of extinction. Our melancholia is being sensed by those who take us very seriously, namely our students, house officers, and fellows" (2). The stark funding realities of today have unfortunately made "prophets out of all those naysayers" to whom Benz referred (2).

Over the years, various organizations have provided reports and recommendations on strengthening the physician-scientist workforce in the United States. However, the requisite follow-up to collect the data that would establish an evidence base of outcomes to promote or refute the utility of the recommendations lags far behind. Combined with the evolving role of the physician-scientist, there is a greater need for a unifying national agenda from all stakeholders to optimize the training and cultivation of physician-scientists in the United States.

In 2008, the Association of Professors of Medicine (APM) published a report recommending an increased focus on repairing the "leaking" physician-scientist pipeline by utilizing a contemporary approach to mentoring physician-scientists, proactively promoting advancement and minimizing attrition of female physician-scientists at an institutional level, and strengthening the physician-scientist workforce by more coordinated efforts to identify and prepare investigators committed to research careers (3). Similarly, in 2014, the NIH published a report with nine major recommendations for sustaining strong support for MD/PhD training, increasing individual fellowship support and granting mechanisms to facilitate independence, and improving tracking of the career development of physician-scientists (4).

In a recent survey of MD/PhD program alumni, 95% entered residency training and 81% were employed in academia, research institutes, or industry (5). This report identified emerging trends that should continue to be monitored, including fewer graduates foregoing residency or holding primary appointments in nonclinical departments; increasing time to graduation; and more diverse residency choices, including a focus on clinical practice rather than research (5). In a 2007 survey, MD/PhD trainees, although generally satisfied with their overall education, reported greatest challenges during the PhD training phase of their programs, indicating need for more guidance and mentoring during this stage (6).

These reports suggest that just as the role of physician-scientists is metamorphosing, so too should their training and development. Ostensibly, the role of the physician-scientist is to advance both clinical practice and scientific inquiry in medicine; however, disparate time demands detract from these pursuits. Since the 1980s, US physicians report that their primary professional activ-

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ity has increasingly been direct patient care, with a concomitant decline in their research activity (7). Competing against full-time researchers for limited funds has led to a steady decline in the number of NIH-funded MDs in medical school basic science departments (stable trend for MD/PhDs), the number of medical school basic science faculty who are MDs (slow upward trend for MD/PhDs), and the number of MDs on NIH review panels (stable trend for MD/PhDs) (7). The waning trends for MDs are complemented by waxing trends for PhDs, raising concern over the diminished role of physician-scientists in research (8). To better prepare for the ever-changing role of the physician-scientist, trainees need formal instruction in skills such as grantsmanship, contract negotiation (including advocating for protected research time and buffering against distractions from the requisite focus on biomedical research), collaborations, managing and staffing a research lab, and budget management. Over the course of the career of a physician-scientist, these are competencies that, if mastered earlier, can pay dividends in complementing the individual's scientific research program.

Recruitment into the pipeline

To better support the future physician-scientist workforce, one needs to look at both the recruitment and retention of trainees (3, 8–12). Currently, the greatest investment in funding and infrastructure has been in the establishment and support of dual degree (MD/PhD and DO/PhD) training programs (5, 13–16). Medical students are also able to pursue limited research training during medical school through research rotations or by taking an additional year to pursue research under established programs hosted by the Howard Hughes Medical Institute, the NIH, the Doris Duke Charitable Foundation, or the Sarnoff Cardiovascular Research Foundation, among others (17–19). However, despite the prevalence of these programs, there has been limited outcomes research to date on their ability to produce successful physician-scientists (20). Outside of these established programs, medical students, residents, and fellows must pursue and struggle on their own to gain the required research experience to become successful physician-scientists (21).

At the undergraduate medical education (UME) level, there is already a dichotomy in the types of students who are chosen for admission into medical schools (11). Medical school admissions vary widely from institution to institution and largely depend on the schools' core missions (16). The foremost priority for schools is the selection of students to become future physicians but not necessarily future physician-scientists. Schools with strong research missions have greater incentive to train physician-scientists and accordingly select students with more intensive research backgrounds (16). In general, medical students should undergo rigorous education in basic science and be more exposed to research opportunities as formal components of their UME (22). Some medical schools, such as the Cleveland Clinic Lerner College of Medicine, Duke University School of Medicine, and Baylor College of Medicine, to name a few, have integrated 12 months of time dedicated to scholarly research activities (23–25). The primary value for future physicians is to instill an understanding of how research is performed and its value, as well as providing the opportunity to further research training at later stages. In comparison to established dual-degree programs, there is limited infrastructure in place to support students to pursue formal research training outside a master's or PhD program, and there are even fewer financial incentives in place to support medical students during those times of lost opportunity cost.

Similarly, at the stage of graduate medical education (GME) including clinical residencies and fellowships, significant research opportunities are not available until the later fellowship years of training. Even at this late stage, it is still realistic to recruit budding physicians into the physician-scientist career pathway, especially those late-blooming individuals who were not previously exposed to formal research training programs. More institutions should support the ability of medical residents and fellows to pursue extensive research opportunities that lead to master's or PhD degrees. This particular stage of training has perhaps the greatest potential as an investment to support individuals toward an independent research career (3, 8). In addition to the traditional financial support during this research training, the NIH loan repayment program should be further expanded, especially for individuals with a large debt burden from medical education (26). Active recruitment and mentorship support for budding physician-scientists at this stage should continue to be more structured to ensure adequate programmatic/administrative support, and more importantly, to ensure research training that is appropriate in content, duration, and caliber. The fact that physician-scientist mentors are critical to cultivating and sustaining the research interests and drive of the physician-scientist trainee cannot be overstated (3, 4, 7–10, 12, 18, 20).

Structure of research training

Over the last few decades, physician-scientists trainees have witnessed a steady increase in the length of time to degree and to research independence. For MD/PhD program graduates, the average time to graduation rose to 8 years (1998–2007) compared with 6.6 years in the 1980s (5). Similarly, the average age at first R01-equivalent award has steadily increased from 37 in 1985 to 44.3 in 2011 for MD/PhDs (27). While these trends reflect the increasing complexity of science and medicine and increasing training required to master both, they lead us to ask whether the 50-year-old MD/PhD training structure is still optimal to support the needs of the physician-scientist workforce.

Current data support the integral role that MD/PhD programs play in the development of successful physician-scientists. Comparatively, MDs tend to be less successful than MD/PhDs in obtaining first-time R01 funding or receiving subsequent R01 grants with similar lengths of training (28). Increased research exposure correlates strongly with retention in the pipeline and securing research-oriented faculty positions (17). Foregoing PhD training as a physician-scientist does not necessarily lead to a decrease in the time to research independence. In 2012, the average age to first research project grant (RPG) was 43.8 for MDs and 44.3 for MD/PhDs (4). The challenge for newer alternative programs is to balance reducing the training time while maintaining the rigor of training. However, current data still support PhD training as the most effective mechanism to develop the physician-scientist workforce.

The next issue is where PhD training would be best situated in the physician-scientist training pipeline. Most MD/PhD students pursue their PhD between the second and third year of medical school, prior to their clinical training and while still undecided about their future medical specialty. Currently, 95% of MD/PhD trainees pursue residency training, and less than 10% of MD/PhDs ultimately have faculty appointments in basic science departments (5). Of the MD/PhD program alumni surveyed, 42.6% conducted clinical research and 41.6% conducted translational research (5). In a previous survey of MD/PhD trainees, students' clinical interests significantly diverged between the start and the end of their MD/PhD training (6). The vast majority of MD/PhDs conduct research closely aligned to their clinical specialties, and most eventually require further patient-oriented research training not necessarily provided by MD/PhD programs (5, 6, 12). While pursuing PhD training earlier imparts important investigative skills, we believe that timing the PhD prior to the clinical "differentiation" of physician-scientists may be prolonging the total training time to independence.

Nesting PhD training within GME, rather than UME, could help eliminate some of the redundancy in the training structure. While it is still important to maintain research exposure and a strong basic science education at the UME level to better prepare budding physician-scientists and expose the physician workforce, we believe that research involvement could be limited to research electives and year-out research programs. By placing their intensive PhD research training closer to the time of research independence, trainees will be far less removed from the research techniques and expertise they have developed. We recognize that this new timing of PhD training would present its own set of recruitment and retention challenges.

Recently, an increasing number of MD/PhD trainees are choosing to pursue residency training in specialties that have not been traditionally pursued by physician-scientists, such as dermatology, ophthalmology, radiation oncology, and surgery (5). The proportion of those pursuing internal medicine, neurology, pathology, and pediatrics (the traditional physician-scientist specialties) has steadily decreased over the past decade (5, 13). This presents a new challenge for specialties where extensive research training infrastructure to support the development of physician-scientists during residency and fellowship is limited or nonexistent (5). We support the establishment of a centralized GME-level institutional physician-scientist training program (PSTP) incorporating all clinical departments, similar in structure to current MD/PhD training programs at the UME level, or alternatively an institution-wide office that would coordinate physician-scientist training at both the UME and GME levels. This central office would provide more structured research training guidance, career development training resources, mentoring, and grant writing support to trainees. Through this office, financial incentives and loan repayment programs could be provided to alleviate the financial burden of prolonging training time during a period when residents/fellows establish families and/or care for elderly parents. By centralizing resources, institutions can provide much better support at a susceptible point in the pipeline that may contribute to the most attrition.

Transition to independence

Over the course of the physician-scientist training period, transition points, especially the last transition to independence, are the most vulnerable to attrition from the pipeline. A significant number of physician-scientists abandon research at the transition from NIH career development award (K) to R funding or when they fail to renew their first R award (28, 29).Like the 2014 NIH (4) and the 2008 APM (3) reports, we also strongly call for increasing the support for physician-scientists at this transition point via the K mechanism and overhauling the structure of the award. The K award should be more flexible for physician-scientists, with a combination of reducing the minimum percent effort from 75% to 50% and lengthening the time period the award covers while maintaining the same cumulative effort as current awards. This would allow physician-scientists the ability to better manage their clinical responsibilities, including medical board licensure. In addition, K awardees and their mentors should be brought together for a mentoring/career development conference hosted by the NIH. Other known issues that need be addressed include formalizing the mentorship structure and compensation, revising the NIH salary pay cap on physician-scientists, and providing better support during the K to R transition.

Participation in K programs has been shown to increase future R01 and RPG success rates. In 2011, the NIH reported that 42% of K08 awardees between 2000 and 2005 subsequently successfully received RPG funding compared with a 21% success rate for non-K08 awardees (30). Similarly, 32% of K23 award recipients subsequently received NIH RPG funding compared with 20% of non-K23 applicants (30). While participation in mentored K award programs increases the likelihood of an independent research career, the success rate still remains relatively low. The report also states that 44% of unfunded K08 applicants and 35% of unfunded K23 applicants have no subsequent interaction with the NIH (30), most likely representing investigators abandoning their independent research careers.

The K99/R00 funding mechanism had a success rate of 23.3% among its awardees in fiscal year 2012 (31), with fewer than 50 MD/PhD applicants and fewer than 25 MD applicants yearly since 2006 (4). A mechanism similar to the K99/R00 award, but specific to physician-scientists with a longer award period and increased salary support, would ensure that trainees have more protected time to be sufficiently prepared to apply for their first independent R award. Increasing salary support and research staff would also make this path more attractive and feasible, especially in specialties with less infrastructure and institutional support for physician-scientist trainees, where the NIH pay cap may be an additional contributing hurdle.

If combined with GME-level PSTPs, applying for a transition to independence via the K/R award can become the capstone of such training programs. Training programs at that stage are best positioned to provide centralized and formal career development, mentoring, and grant writing support to ensure a smoother transition to independence. Similar programs at the junior faculty level have already been implemented, such as the Vanderbilt Physician-Scientist Development Program (VPSD), an NIH-funded program that provides salary support and additional mentored investigative training to newly appointed assistant professor physicians with significant research experience. Early outcomes data reveal increased physician-scientist retention rates and increased K award success funding rates (32). Unfortunately, these institutional programs are rare. Most physician-scientists cross the bridge to independence with limited support and resources, relying on informal mentoring structures to navigate the chasm to research independence. Without a stable and supportive infrastructure in place, it is not surprising that many are discouraged and/or fail.

There also need to be formal mentoring structures as part of K/R awards, accompanied by appropriate metrics for assessing the effectiveness of such structures. For instance, in *The Vanishing Physician-Scientist?*, Andrew Schafer calls for mentoring committees for physician-scientists that provide trainees with access to a wide range of mentoring resources and a broad pool of expertise critical in today's interdisciplinary research landscape (8). In addition to mentoring, these awards should provide a career development component for trainees to receive training on practical skills that contribute to the success of the physician-scientist workforce.

Our recommendations

There is an urgent need to reinvigorate the physician-scientist workforce and to address the challenges facing it. We believe that restructuring training to reduce the total training time and establishing more formalized support at the transition to independence are vital steps in preserving the pipeline of successful physician-scientists.

We recommend that all medical schools include a substantive introductory research experience as part of UME. Further, we posit that incorporating intensive research training at the GME level would better position physician-scientists for ultimate success, allowing individuals to focus their research training and investigations in their area of clinical specialty and to more seamlessly transition from training to independence. To facilitate training during this period, we propose the establishment of a centralized GME-level physician-scientist training program or, alternatively, an institution-wide office that would coordinate physician-scientist training at both the UME and GME levels. This office should provide trainees with formal instruction in non-research skills required for success, including grant writing, contract negotiation, and research lab management. The office would be positioned to provide active recruitment and mentorship support for budding physician-scientists.

In addition to changes at the institutional level, we believe that changes to support mechanisms are also needed. The NIH loan repayment program should be expanded to support more physicians pursuing research degrees at the GME level. We strongly advocate for increasing support and the period of eligibility by relaxing the percent time effort requirement and lengthening the award period for NIH K awards for physician-scientists to better facilitate their final transition to independence. The K and R awards for young independent researchers should also include a more formal mentoring structure, and a required mentoring/career development conference for the awardees and their mentors.

Any changes made to the training programs or award mechanisms for physician-scientists must include follow-up studies to determine the efficacy of policy changes. Only by close examination of outcomes data can we be certain that efforts to improve the recruitment and retention of physician-scientists are optimized for the current research era.

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